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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/326,402	06/04/1999	MARTA BLUMENFELD	GENSET.030A	4132

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EXAMINER	
MAHATAN, CHANNING	
ART UNIT	**PAPER NUMBER**
1631	30

DATE MAILED: 05/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/326,402	BLUMENFELD ET AL.	
	Examiner	Art Unit	
	Channing S. Mahatan	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *89-182* is/are pending in the application.

4a) Of the above claim(s) *89-120,142-149 and 153-162* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *121-141,150-152 and 163-182* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *89-182* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *04 March 2003* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

APPLICANTS' ARGUMENTS

Applicants' arguments in Paper No. 28, filed 04 March 2003, have been fully considered but they are not deemed to be persuasive for the reasons set forth below. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

SEQUENCE COMPLIANCE

The following sequence compliance issue regarding Figures 7A-D is reiterated from the previous office action:

> 4. Each sequence in the specification is required to have a SEQ ID NO. therewith. It should be noted that SEQ ID NOs. are not required in the Figures per se, but may be set forth in the Brief Description of the Drawings section.

Applicants are given the same response time regarding this failure to comply as that set forth to respond to this office action. A complete response to this office action includes compliance with this sequence rule compliance requirement. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this office action.

CLAIMS UNDER EXAMINATION

Claims herein under examination are claims 121-141, 150-152, 163-182, and SEQ ID NO. 12 in its entirety; including all variable positions (biallelic marker positions 402, 8187, 34266, 67092, 68525, 82234, 82393) have been examined. Claims 89-120, 142-149, and 153-162 remain withdrawn as not directed to the elected subject matter and all sequences other than the elected SEQ ID NO. 12 remain withdrawn.

OBJECTION TO SPECIFICATION

The amendment in Paper No. 28, filed 04 March 2003, is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material, which is not supported by the original disclosure, is as follows:

> "SEQ ID NO: 12 contains a genomic sequence of PCTA-1 comprising the 5' regulatory region (upstream untranscribed region), the exons (0, 1, 2, 3, 4, 5, 6, 6bis, 7, 8, 9, 9bis, and 9ter) and introns, and the 3' regulatory region (downstream untranscribed region). This sequence is identical to that of SEQ ID NO: 1 and these SEQ ID NOs may be used interchangeably throughout the subject application."

Applicants' state in Paper No. 28, filed 04 March 2003, that they have attended to the objection to disclosure regarding the identical nature of SEQ ID NOs. 1 and 12 by indicating that these sequences are identical and that SEQ ID NO.1 and SEQ ID NO. 12 can be used interchangeably throughout the specification. The original disclosure indicated 1) SEQ ID NO. 1 contains a genomic sequence of PCTA-1 comprising the 5' regulatory region (upstream untranscribed region), the exons (0, 1, 2, 3, 4, 5, 6, 6bis, 7, 8, 9, 9bis, and 9ter) and introns, and the 3' regulatory region (downstream untranscribed region)(page 5, lines 8-10); 2) SEQ ID NO. 1 is a DNA sequence of the length 106,746 nucleotides and denotes numerous allele locations

and polymorphic base substitutions (Sequence Listing); and 3) SEQ ID NO. 12 is a DNA sequence of the length 106,746 nucleotides and denotes allele locations and polymorphic base substitutions (positions 402, 8187, 34266, 67092, 68525, 82234, 82393) (Sequence Listing). While it is acknowledged that SEQ ID NO. 12 contains appropriate symbols (i.e. Sequence Listing; allele substitutions at nucleotide positions 402, 67092, 68525, 82234, and 82393 as in SEQ ID NO. 1, the sequences are not considered identical and are not interchangeable. SEQ ID NO. 1 contains numerous alleles with corresponding nucleotide substitutions that are absent from SEQ ID NO. 12, for example, positions 278, 472, 100, etc. Therefore, the introduction of the above amendment to the specification is considered NEW MATTER.

Applicants are required to cancel the new matter in the reply to this Office Action.

Therefore, the disclosure remains objected to because of the confusion, which exists between elected SEQ ID NO: 12 and SEQ ID NO: 1. Applicants' are requested to amend the specification to remove the confusion.

Claims Rejected Under 35 U.S.C. 112 1st Paragraph

SCOPE OF ENABLEMENT

Claims 121-141, 150-152, and 163-182 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for a method of identifying a nucleotide (species position 67092 of the elected SEQ ID NO: 12) at a PCTA-1 biallelic marker (A30, allele T, p value = 0.033) in familial prostate cancer, biallelic marker combinations for familial cases of prostate cancer (Table 5; 26 combinations), and biallelic marker combinations for sporadic prostate cancer (Table 6; 18 combinations) does not reasonably provide enablement for the identification of other nucleotides at other PCTA-1 biallelic markers in familial prostate

cancer (i.e. A2, A41, etc), sporadic prostate cancer (i.e. A2, A30, etc.), or in all other combinations. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Again, it is noted that applicants have disclosed that significant p values are preferably less than .01, (page 110, lines 6-13 of the Specification).

Applicants argue in Paper No. 28, filed 04 March 2003, "haplotype association analysis that combines the A2 marker with other markers disclosed in the specification does provide for statistically significant associations of the haplotypes with familial and sporadic cancer". Additionally, Applicants submit that the enablement rejection was improperly applied to claims 131-141. It is noted applicants have failed to present arguments directed to biallelic markers with regards to statistical significance individually and to other biallelic markers (markers not disclosed in Tables 5 and 6) as indicated in Paper No. 26, mailed 23 August 2002, which are encompassed by the instant claim language.

With respect to the application of the "Enablement Rejection" to claims 121-141, 150-152, and 163-182 the below grouping of claims serve to distinguish the varying methods claimed and is followed by an explanation for all grouping by providing for clarification with respect to the recitation of "biallelic marker" applicable to all groups:

Claims 121-130, 151, 152, and 172-176 is drawn to a method of genotyping.

Claims 131 and 167 drawn to a method of estimating frequency of an allele.

Claims 132, 136-141, and 168 drawn to a method of detecting an association between a genotype and a trait.

Claims 133, 134, 169, and 177-182 drawn to a method of estimating the frequency of a haplotype for a set of biallelic markers in a population.

Claims 135, 163-166, and 170 drawn to a method of detecting an association between a haplotype and a trait.

Claims 150 and 171 drawn to a method of determining whether an individual is at risk of developing prostate cancer.

The recitation of "biallelic marker" implies more than just the sequencing of the "PCTA-1-related biallelic marker". The underlying issue is the "statistically significant" values exemplified by the original disclosure (i.e. Tables 5 and 6) that would enable one of skill in the art to practice the claimed invention(s). It is these "statistically significant" values in sporadic and familial prostate cancer that have been assessed, accordingly, with the claimed invention. No other "biallelic marker" and/or "PCTA-1-related biallelic markers other than the ones originally disclosed (i.e. Table 5 and 6) have been shown to be "statistically significant" as a "PCTA-1-related biallelic" to be utilized in the various methods of genotyping, estimating allele frequency, detecting association between a genotype and a trait, estimating halpotype frequency, detecting association between a haplotype and trait, and the determination of whether an individual is at risk of developing prostate cancer. Further, the term "trait" in claims 132 (lines 1, 3, and 7), 135 (lines 1, 3, and 8), 140 (line 2), and 165 (line 1) fails to limit the scope of the invention to the traits (i.e. sporadic and familial prostate cancer) exemplified in the disclosure. Again, no other traits have been shown to be associated with "statistical significance" with the PCTA-1-related biallelic marker(s) in Tables 5 and 6, other than sporadic and familial prostate cancer.

LACK OF WRITTEN DESCRIPTION

Applicants submit in Paper No. 28, filed 04 March 2003, that the rejection is moot in view of the amendments made to the claims and the arguments presented in the traversal of the rejections set forth under 35 U.S.C. § 112 2nd Paragraph.

The rejection of claims 121-141, 150-152, and 163-182 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention are maintained for reasons of record (Refer to 112 2nd Paragraph Rejections).

Claims Rejected Under 35 U.S.C. 112 2nd Paragraph

Claims 121-141, 150-152, and 163-182 are rejected under 35 U.S.C. § 112 2nd Paragraph as necessitated by amendment. Additionally, for reasons of record the rejections of claims 121-141, 150-152, and 163-182 under 35 U.S.C. § 112 2nd Paragraph as indicated in Paper No. 26, mailed 23 August 2002, are maintained.

VAGUE AND INDEFINITE

Claims 121-141, 150-152, 163-182 are confusing as written because they embrace more than the elected invention. Applicants are reminded of the election of SEQ ID NO. 12 in Paper No. 25, filed 11 March 2002. Applicants are requested to amend the claims so that they reflect the elected invention. Note that it is difficult to evaluate the claims for enablement because the language used does not reflect the invention being examined. The examiner cannot anticipate the final form of the claims.

Claims 121 (line 2), 131 (line 1), 132 (lines 3 and 5), 133 (line 3), 150 (line 3), 151 (line 1), 152 (line 1), 167 (line 1), 168 (line 1), 169 (line 1), 170 (line 1), 171 (line 1), 172 (line 1), 177 (lines 1 and 2), 178 (lines 1 and 2), and all claims dependent therefrom are vague and indefinite as to what is meant therein by the limitation "PCTA-1-related biallelic marker". Applicants submit that the claims would not be vague or indefinite to one of ordinary skill in the art pointing to page 11, lines 22-25 wherein the term PCTA-1 related biallelic marker relates to a set of biallellic markers in linkage disequilibrium with the PCTA-1 gene. It is note the specification states on page 11, lines 24-25, the "term PCTA-1 related biallelic marker encompasses all of the biallelic markers A1 to A125 disclosed in Table 2". The term "encompasses" provides for an unlimiting definition as to PCTA-1 related biallelic markers and/or marker in general. Thus, the claims fail to provide appropriate limitations as provided for by the specification, wherein the specification provides for a broad range of biallelic markers as indicated by the term "encompasses". Applicants can resolve this issue by particularly pointing out the metes and bounds of "related", via clearer claim language.

Claims 121, 140, 151, 152, 167-172, 177, 178, and all claims dependent therefrom are vague and indefinite as to what is meant therein by the limitation "the complement". Applicants submit in Paper No. 28, filed 04 March 2003, that the phrase "the complement" is fully understandable in the context of the claimed invention, one skilled in the art would recognize that the phrase "complement thereof" relates to nucleotides identified as the biallelic markers of the elected sequence, and have amended the claims to more distinctly identify that such is the case, which is found unpersuasive. The following is reiterated from the previous office action:

> A possible interpretation is that the complement must be of the same length and be the full and exact complement of the recited SEQ ID NO. sequence. Another

interpretation is that any complement is meant including those with less than 100% complementarity, such as 90%, 50%, or even 10%. Clarification of the metes and bounds of the claim is requested via clearer claim wording.

Claims 150 (lines 1-2) and all claims dependent therefrom are indefinite due to the lack of clarity of the claim language failing to recite a final process step, which agrees back with the preamble. Applicants submit in Paper No. 28, filed 04 March 2003, that the rejection is moot in view of the amendments made to the claim, which is found unpersuasive. The preamble states that it is "a method of determining whether an individual is at risk of developing prostate cancer", however the claim recites a final step of correlating the result of the step a) with a risk of developing prostate cancer. The claim does not set forth the conditions/state when in any of the claim steps that such "risk is determined". While minor details are not required in method/process claims, at least the basic step must be recited in a positive, active fashion. For example, what level of correlation is required to be associated with the stated risk. Clarification of the metes and bounds of the claim is requested via clearer claim wording.

LACK OF ANTECEDENT BASIS

Claim 140 (line 2) recites the phrase "control population" which lacks antecedent basis from claim 132. Applicants submit in Paper No. 28, filed 04 March 2003, that the term "control population" can be found in step b) of claim 132, which is found unpersuasive. It is acknowledged that claim 132 (line 5) recites "control", however lacks any indication that said control is a "control population".

Claim 141 (line 1) recites the phrase "case control population" which lacks antecedent basis. Applicants submit in Paper No. 28, filed 04 March 2003, that this rejection is moot in

view of the amendment made to the claims. Again it is acknowledged that claim 132 (line 5) recites "control", however lacks any indication that said control is a " case control population.

ACTION IS FINAL AS NECESSITATED BY AMENDMENT

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Appropriate Correction Is Required.

No Claims Are Allowed.

EXAMINER INFORMATION

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and

1157 OG 94 (December 28, 1993) (See 37 C.F.R. § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Channing S. Mahatan whose telephone number is (703) 308-2380. The examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina M. Plunkett, whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

Date: May 19, 2003

Examiner Initials: CSM

Marianne P. Allen

MARIANNE P. ALLEN
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